PHARMACOLOGY

INTRODUCTION & ADME

ملخص مادة علم الأدوية المحاضرة الأولى + والثانية

إعداد/

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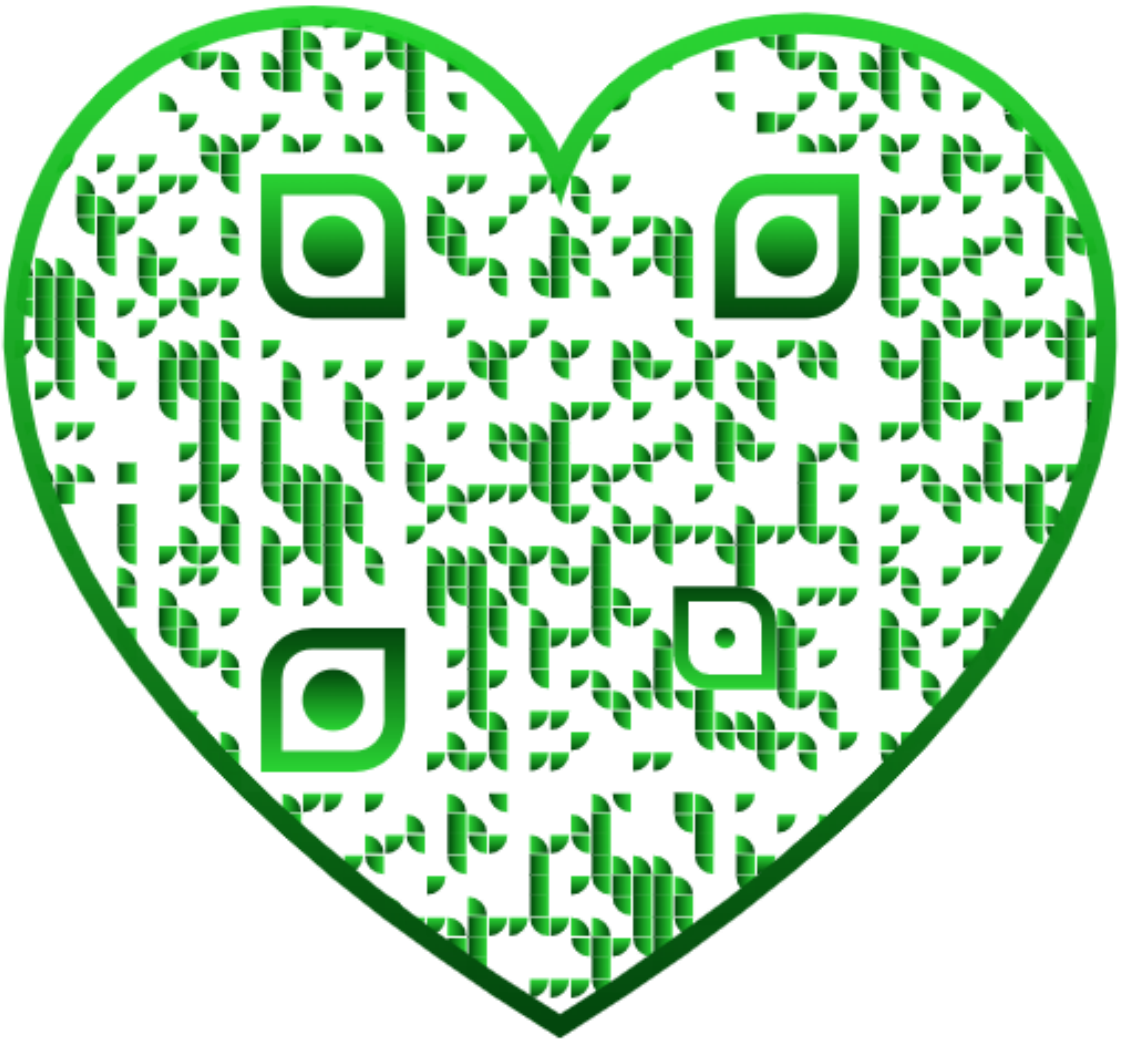
بلال جعوان

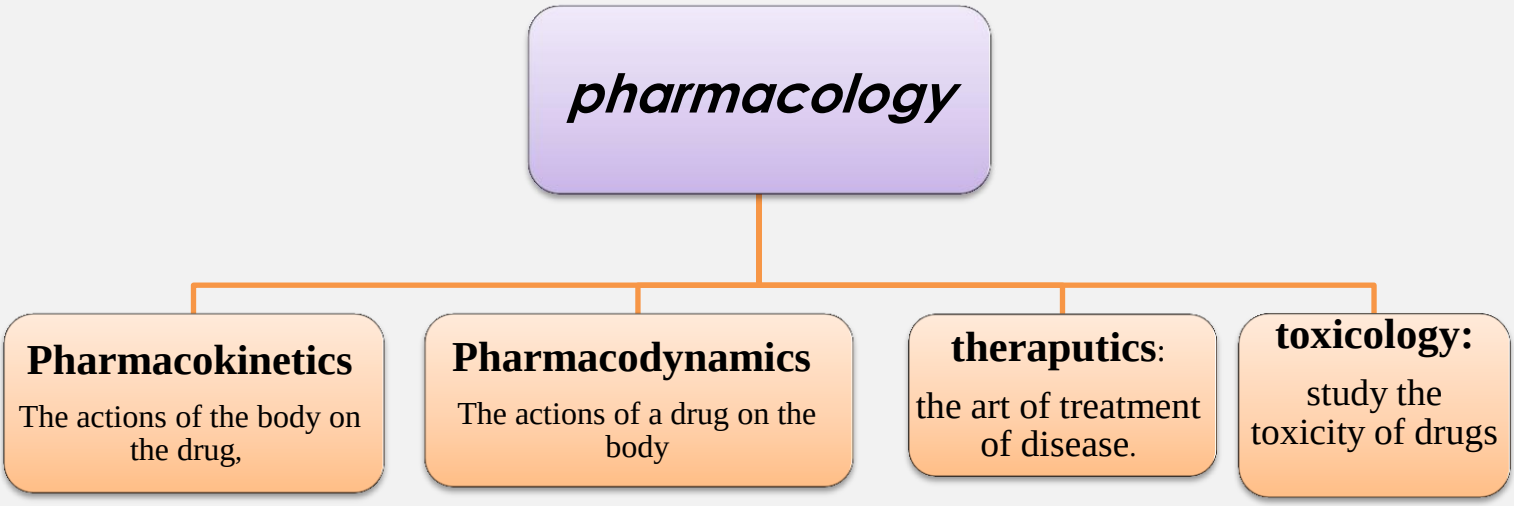


INTRODUCTION

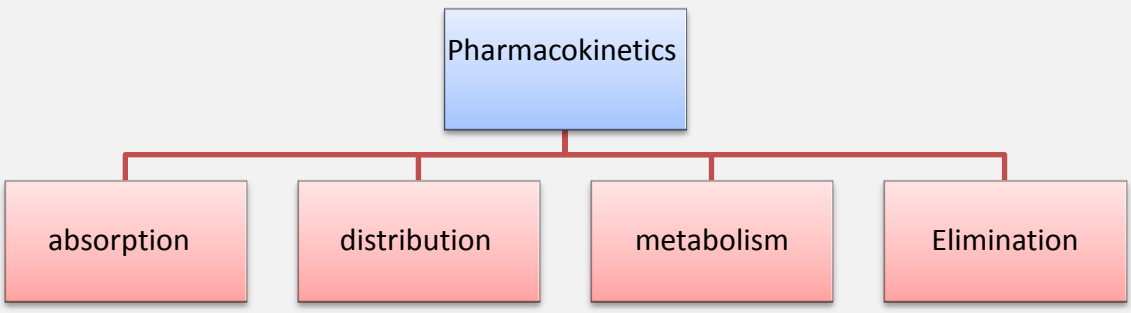
What is the pharmacology?

It is the science of the drug.

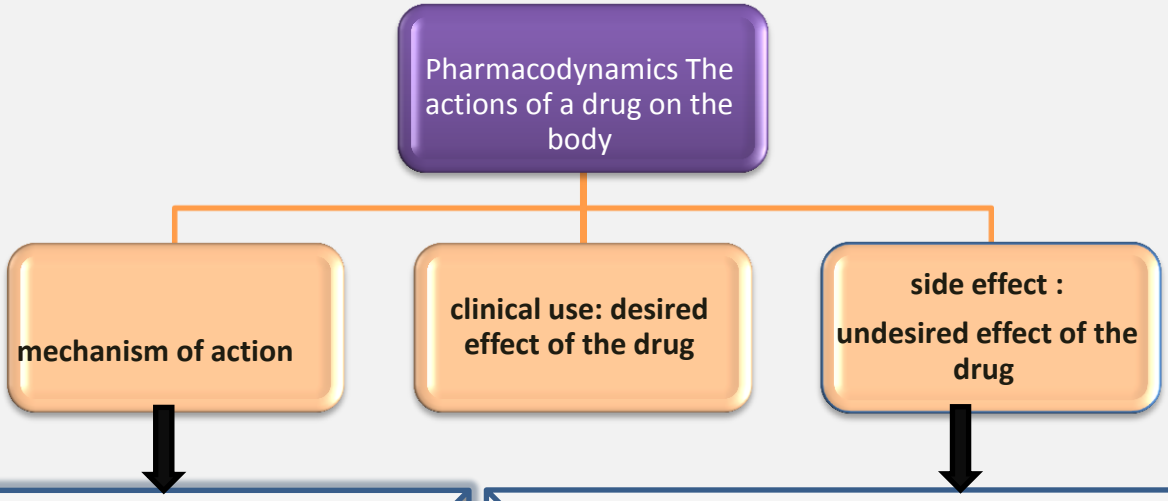
Science of pharmacology



1) Pharmacokinetics



2) Pharmacodynamics


Pharmacodynamics The actions of a drug on the body
mechanism of action
clinical use: desired effect of the drug
side effect : undesired effect of the drug

- DNA : anti-viral
- cell membrane
- : anti-bacterial, anti-fungal
- receptor: part of cell chemically active
- enzymes: ion channel ,Na+,Ca+,.. .
- chemical reaction : anti-acid compound(neutralization)in stomach.
- physical reaction: adsorbent, charcoal to toxic substance.

Tolerance:

It is the need to increase the drug dose to get the same response

Tachyphylaxis

Rapid occurrence to tolerance e.g. (analgesic or drug).

Dependence Severe craving to drug in which sudden stop cause central withdrawing effect cause symptoms (angry, agitation, aggressive)but B.P (blood pressure) and blood sugar is normal, treatment gradually.
e.g.(DIAZEPAM).

Addiction:

more severe craving in which sudden stop cause physiological & psychological effect on CNS & PNS (withdrawing effect) may cause death.

-Hard treatment because it needs a hospital to convert addiction to dependence of stopped gradually

e.g. (Morphine).

3) Therapeutics

*Is the art of treatment of disease. **Mean:** the proper drug to proper dose to proper disease.*

e.g. elderly has headache
adult has a headache } not the same drug

elderly has renal failure
adult has renal failure } not the same drug

4) Toxicology

Is the study of the toxicity of the drug. Toxic dose
toxic symptoms (side effect)
treatment of toxicity

What is the pharmacology?

It is the science of the drug

Drug: any substance from natural or synthetic source that have a pharmacological effect.

Or
Compounds that interact with biological membrane to produce a biological response.

Natural source of the drug

1)Plant: senna, e.g. hyocine, atropine belladonna

2)Animal: insulin

3)microorganism: cod liver oil, marine.

Synthetic : penicillin, aspirin,…. . **cheep**

ROUTES OF DRUG ADMINISTRATION

- Enteral
  - Oral
  - Sublingual/buccal
- Parenteral
  - Intravenous (IV)
  - Intramuscular (IM)
  - Subcutaneous (SC)
- Other
  - Oral inhalation:
  - Nasal inhalation
  - Intrathecal/intraventricular
  - Topical
  - Transdermal:
  - Rectal:

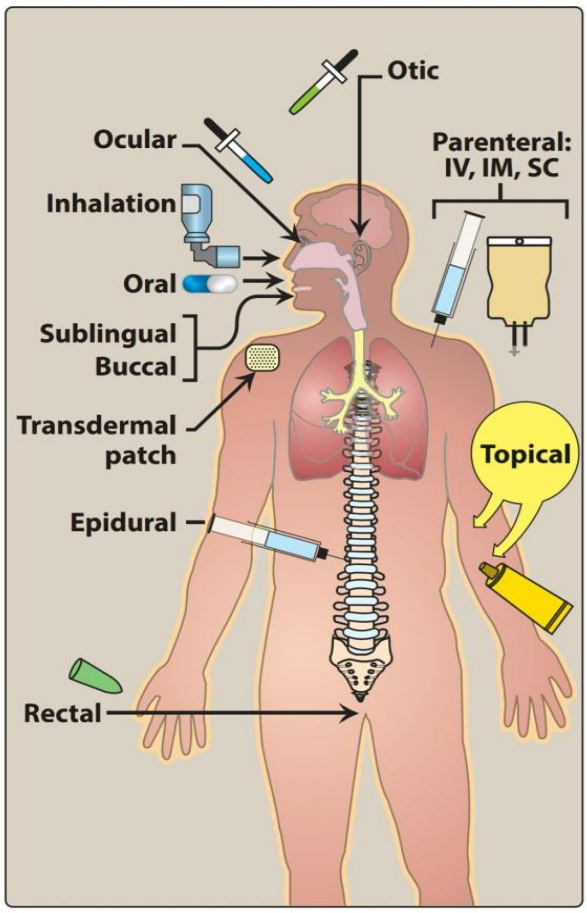


Figure 1.2
Commonly used routes of drug administration. IV = intravenous; IM = intramuscular; SC = subcutaneous.

Important difinitions

AGONIST

compound which bind to sympathetic receptor & produce similar effect to those of natural neurotransmitter, e.g.

Antagonist

compound which bind to sympathetic receptor & produce opposite effect to those of natural neurotransmitter.

Therapuetic index (TI)

It is the degree of drug safty.

$$TI = \frac{TD\ txic\ dose}{ED\ effective\ dose} = \frac{50}{50}$$

Potency

It is the strength concentration of the drug.

Efficacy

It is the maximum amount of response produced by drug.

There are two terms related to efficacy & potency more effective & more potent respectively.

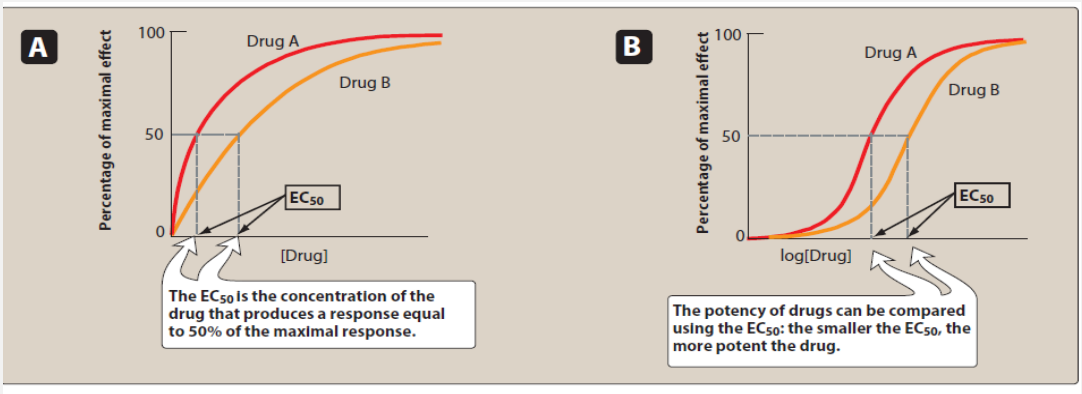


Figure 2.7
The effect of dose on the magnitude of pharmacologic response. **Panel A** is a linear graph. **Panel B** is a semilogarithmic plot of the same data. EC_{50} = drug dose causing 50% of maximal response.

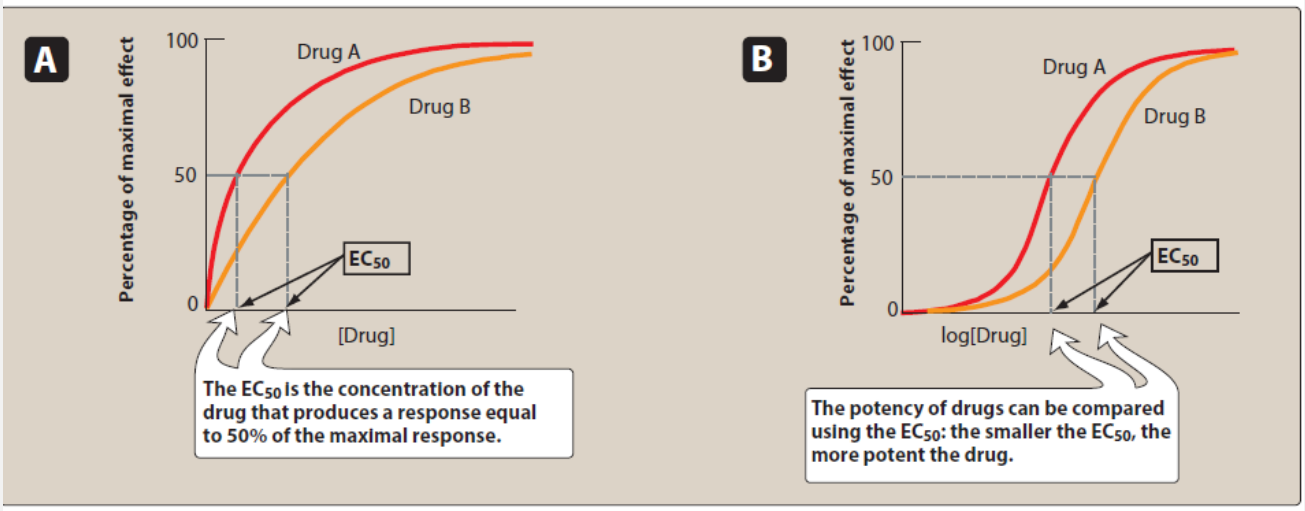
Drug Response

It is the effect of the drug on the body.

Drug monitoring

Mesurement the effect of the drug. E.g. parameter measure the glucose in the blood,

Measuring concentration of drug in the blood e.g. symptom: disappear of symptoms of headache.



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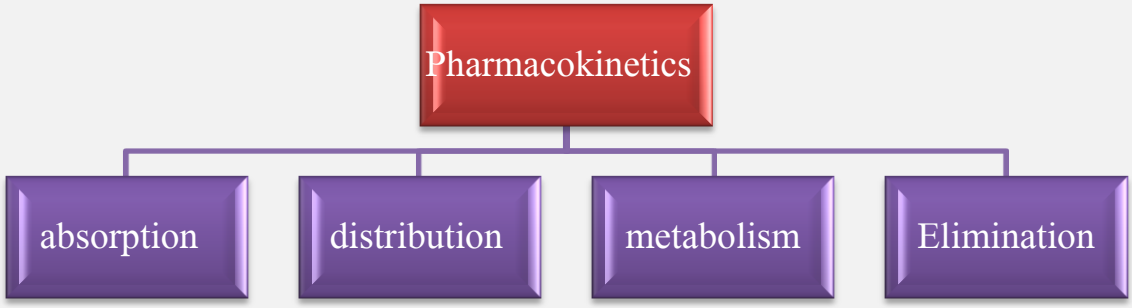
Pharmacokinetics

Pharmacokinetics *denotes the effects of biologic systems on drugs. The major processes involved in pharmacokinetics are absorption, distribution, metabolism and elimination.*



I. ABSORPTION OF DRUGS:

is the transfer of a drug from the site of administration to the bloodstream.

The rate and extent of absorption depend on the environment where the drug is absorbed, chemical characteristics of the drug, band the route of administration (which influences bioavailability).

Routes of administration other than intravenous may result in partial absorption and lower bioavailability.

Bioavailability is the rate and extent to which an administered drug reaches the systemic circulation.

$$\times \text{ bioavailability} = \frac{concentration\ of\ drug\ in\ blood}{concentration\ of\ drug\ administrated} \times 100$$

For example, if 100 mg of a drug is administered orally and 70 mg is absorbed unchanged, the bioavailability $= \frac{100mg}{70mg} \times 100 = 70\%$

the bioavailability is 0.7 or 70%.

↑ Bioavailability of drug --- ↑ highly absorption more effect.

↓ Bioavailability of drug --- ↓ poor absorption less effect.

Sites of absorption ***main in the small intestine.***

Factors affecting on absorption

Related to patient

Factors affecting on absorption

Related to patient

*1)**presence of food 90% cause poor absorption**.*

*2)**health state**.(if patient has a diaohrea there is not enough time to absorption of drug from intestine but in conistbation more absorption occurs.*

Related to drug

1) lipid soluble

drug which is more soluble --- absorption

drug which is soluble is absorption

2) particle size

Drug with large PZ will have low solubility therefore low absorption

*3) **the dosage form***

Liquid dosage form is more absorption than solid dosage form.

*4) **rout of administration***

Parenteral more than Oral more than topical.

4) More blood supply more absorption e.g. Sublingual TAB

DRUG DISTRIBUTION

Drug distribution

Is the spread of the drug all over the body, *DRUG* bind o plasma protein.

Increase of binding drug --- decrease the activity of the drug.

Decrease of binding drug--- increase the acivity of the drug.

DRUG METABOLISM

First step in drug elimination which occurs mainly in the liver.

NOTE

"**Elimination**" mean stop the effect of the drug.

" **REMOVAL**" take out of the drug from the body.

Metabolism cause chemical modification change chemical active group of drug by increasing the polarity to be easly excreted from the body.

1. ***Convertion of drug from non-polar to polar (e.g. ASPIRIN)***
2. ***Connvertion of drug from active to inactive.***
3. ***Convertion of drug from inactive to active. (e.g.CLOPIDOGREL)***
4. ***Connvertion of drug from active to active. (e.g.DIAZEPAM)***
5. ***Connvertion of drug from active to toxic. . (e.g.PARACETAMOL)***

SITES OF METABOLISM:

1) ***Mianly in the liver.***
2) ***In the blood by enzymes e.g. esterase.***
3) ***In kidnys***
4) ***In lungs***

Facctors affecting on liver metabolism

1) Health state of liver (hepatic failure need drug completely soluble)
2) Age increase enzyme till eldery.
3) Sex (male more than famale because of testoesteron).
4) Drug-drug interaction.

Drug-drug interaction

Metabolic inducers

Drug that stimulate metabolism e.g. phenytoin

Metabolic inducer drugs if taken with other drugs should have interval because Metabolic inducer drugs decrease the activity of the other drugs.

Metabolic inhibitors

Drugs decrease metabolism e.g. (erythromycin)

Metabolic inhibitor drugs if taken with other drugs prevent their metabolism & cause toxicity.

DRUG EXCRITION

Removal of the drug outside of the body.

Sites :

1) Kidneys mainly 90%.
2) GIT 10%.
3) Saliva.
4) Sweating.
5) Respiration.
6) Lacrimation.

Factors affecting on drug excretion

-Health state of kidneys.

-Polarity of the drugs.

TABLE 6–4 Steps in autonomic transmission: effects of drugs.

Process	Drug Example	Site	Action
Action potential propagation	Local anesthetics, tetrodotoxin,[a] saxitoxin[b]	Nerve axons	Block sodium channels; block conduction
Transmitter synthesis	Hemicholinium	Cholinergic nerve terminals: membrane	Blocks uptake of choline and slows synthesis of acetylcholine
	Alpha-methyltyrosine (metyrosine)	Adrenergic nerve terminals and adrenal medulla: cytoplasm	Slows synthesis of norepinephrine
Transmitter storage	Vesamicol	Cholinergic terminals: vesicles	Prevents storage, depletes
	Reserpine	Adrenergic terminals: vesicles	Prevents storage, depletes
Transmitter release	Many[c]	Nerve terminal membrane receptors	Modulates release
	ω-Conotoxin GVIA[d]	Nerve terminal calcium channels	Reduces release
	Botulinum toxin	Cholinergic vesicles	Prevents release
	Alpha-latrotoxin[e]	Cholinergic and adrenergic vesicles	Causes explosive release
	Tyramine, amphetamine	Adrenergic nerve terminals	Promotes release
Transmitter uptake after release	Cocaine, tricyclic antidepressants	Adrenergic nerve terminals	Inhibit uptake; increase transmitter effect on postsynaptic receptors
	6-Hydroxydopamine	Adrenergic nerve terminals	Destroys the terminals
Receptor activation or blockade	Norepinephrine	Receptors at adrenergic junctions	Binds α receptors; causes activation
	Phentolamine	Receptors at adrenergic junctions	Binds α receptors; prevents activation
	Isoproterenol	Receptors at adrenergic junctions	Binds β receptors; activates adenylyl cyclase
	Propranolol	Receptors at adrenergic junctions	Binds β receptors; prevents activation
	Nicotine	Receptors at nicotinic cholinergic junctions (autonomic ganglia, neuromuscular end plates)	Binds nicotinic receptors; opens ion channel in post-synaptic membrane
	Hexamethonium	Ganglionic nicotinic receptors	Prevents activation of N_N receptors
	Tubocurarine	Neuromuscular end plates	Prevents activation of N_M receptors
	Bethanechol	Parasympathetic effector cells (smooth muscle, glands)	Binds and activates muscarinic receptors
	Atropine	Parasympathetic effector cells	Binds muscarinic receptors; prevents activation
Enzymatic inactivation of transmitter	Neostigmine	Cholinergic synapses (acetylcholinesterase)	Inhibits enzyme; prolongs and intensifies transmitter action
	Tranylcypromine	Adrenergic nerve terminals (monoamine oxidase)	Inhibits enzyme; increases stored transmitter pool

[a]Toxin of puffer fish, California newt.